

d his

(FILE 'HOME' ENTERED AT 16:28:30 ON 24 MAR 2004)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
16:28:52 ON 24 MAR 2004

L1 165 S (NUCLEIC ACID APTAMER)
L2 22 S L1 AND POLYMERASE?
L3 21 DUPLICATE REMOVE L2 (1 DUPLICATE REMOVED)

=>

updated
search
dates no good.

W/Cook 3/24/04
no GPCR

146484-58-4 146484-59-5 146484-61-9 146484-62-0 146484-63-1
146484-64-2 146484-65-3 146484-66-4 146484-67-5 146484-68-6
146484-69-7 146484-70-0 146484-71-1 146484-72-2 146870-92-0D,
derivs. 146870-94-2 149498-54-4 149498-55-5 149498-56-6
149498-57-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin binding and inhibition by)

IT 126320-34-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-binding and -inhibiting oligonucleotides contg.)

IT 10043-66-0 10098-91-6 15715-08-9 15750-15-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-binding and -inhibiting oligonucleotides labeled with)

IT 14133-76-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-binding and -inhibiting oligonucleotides labeled with metastable)

IT 50-99-7, D-Glucose 59-23-4, D-Galactose 617-04-9 1811-31-0
7512-17-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-oligonucleotide complexes dissocn. from immobilized lectin with)

L6 ANSWER 109 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1993:512963 CAPLUS
 DN 119:112963
 ED Entered STN: 18 Sep 1993
 TI **Aptamers** specific for biomolecules and method of making them
 IN Toole, John J.; Griffin, Linda C.; Bock, Louis C.; Latham, John A.;
 Muenchau, Daryl Dean; Krawczyk, Steven
 PA Gilead Sciences, Inc., USA
 SO PCT Int. Appl., 83 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C12Q001-68
 ICS C07H015-12; C07H017-00
 CC 9-14 (Biochemical Methods)
 Section cross-reference(s): 1, 3

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9214843	A1	19920903	WO 1992-US1383	19920221
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
	CA 2104698	AA	19920822	CA 1992-2104698	19920221
	AU 9214354	A1	19920915	AU 1992-14354	19920221
	EP 572529	A1	19931208	EP 1992-907174	19920221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	JP 06508022	T2	19940914	JP 1992-507073	19920221
	US 5582981	A	19961210	US 1994-234613	19940428
	US 5840867	A	19981124	US 1994-237973	19940503
PRAI	US 1991-658796		19910221		
	US 1991-658849		19910221		
	US 1991-659103		19910221		
	US 1991-659113		19910221		
	US 1991-659114		19910221		
	US 1991-659980		19910221		
	US 1991-659981		19910221		
	US 1991-744870		19910814		
	US 1991-745215		19910814		
	US 1991-787921		19911106		
	WO 1992-US1383		19920221		

AB A method for identifying oligomer sequences which specifically bind target
 mols. (serum proteins, kinins, eicosanoids, etc.) is described. The
 technique involves complexation of the target mol. with a mixt. of
 oligonucleotides contg. random sequences and sequences which serve as
PCR primers under conditions in which a complex is formed with the
 specifically binding sequences, but not with the other members of the
 oligonucleotide mixt. The complex is then sepd. from uncomplexed
 oligonucleotides, and the complexed members of the oligonucleotide mixt.
 are recovered from the sepd. complex using **PCR**. The recovered
 oligonucleotides may be sequenced, and successive rounds of selection
 using complexation, sepn., amplification, and recovery can be employed.
 The oligonucleotides can be used for therapeutic and diagnostic purposes.
 The method is used to generate **aptamers** that bind serum factor
 X, thrombin, bradykinin, and prostaglandin F2.alpha.. **Aptamer**
 specificity for binding to and inhibition of thrombin was demonstrated.
 ST **aptamer** oligonucleotide prepn; blood coagulation factor X
aptamer; thrombin **aptamer**; bradykinin **aptamer**;
 prostaglandin F2 **aptamer**
 IT Immunomodulators
 (**aptamer** conjugates as)

IT Aflatoxins
 Carbohydrates and Sugars, biological studies
 Eicosanoids
 Peptides, biological studies
 Polysaccharides, biological studies
 Proteins, biological studies
 Steroids, biological studies
 Glycerides, biological studies
 Glycolipids
 Glycoproteins, biological studies
 Glycosaminoglycans, biological studies
 Lipids, biological studies
 Monosaccharides
 RL: ANST (Analytical study)
 (**aptamer** oligonucleotide binding to)

IT Diagnosis
 (**aptamers** for)

IT Deoxyribonucleic acids
 RL: ANST (Analytical study)
 (**aptamers**, for binding biomols.)

IT Pharmaceuticals
 (conjugates, with **aptamers**)

IT Ligands
 RL: ANST (Analytical study)
 (for cell surface receptors, immunomodulatory conjugates,
aptamers in relation to)

IT Polymerase chain reaction
 Reducing agents
 (in **aptamer** prepn.)

IT Receptors
 RL: ANST (Analytical study)
 (of cell surface, ligands for, immunomodulatory conjugates,
aptamers in relation to)

IT Immobilization, biochemical
 (of target mol., in **aptamer** prepn.)

IT Agglutinins and Lectins
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (solid support contg., in **aptamer** prepn.)

IT Albumins, biological studies
 RL: BIOL (Biological study)
 (thrombin **aptamer** binding activity for)

IT Antigens
 RL: ANST (Analytical study)
 (CD4, **aptamer** oligonucleotide binding to)

IT Glycophosphoproteins
 RL: BIOL (Biological study)
 (E-selectins, **aptamer** oligonucleotide binding to)

IT Histocompatibility antigens
 RL: BIOL (Biological study)
 (HLA, **aptamer** oligonucleotide binding to)

IT Glycoproteins, specific or class
 RL: BIOL (Biological study)
 (ICAM-1 (intercellular adhesion mol. 1), **aptamer**
 oligonucleotide binding to)

IT Glycoproteins, specific or class
 RL: BIOL (Biological study)
 (ICAM-2 (intercellular adhesion mol. 2), **aptamer**
 oligonucleotide binding to)

IT Glycoproteins, specific or class
 RL: BIOL (Biological study)
 (P-selectins, **aptamer** oligonucleotide binding to)

IT Sialoglycoproteins

RL: ANST (Analytical study)
 (VCAM-1 (vascular cell adhesion mol. 1), **aptamer**
 oligonucleotide binding to)

IT Molecules
 (biochem., **aptamer** oligonucleotides binding to)

IT Animal growth regulators
 RL: ANST (Analytical study)
 (blood platelet-derived growth factors, .alpha.-, **aptamer**
 oligonucleotide binding to)

IT Animal growth regulators
 RL: ANST (Analytical study)
 (blood platelet-derived growth factors, .beta.-, **aptamer**
 oligonucleotide binding to)

IT Antibodies
 RL: ANST (Analytical study)
 (conjugates, immunomodulatory, **aptamer** in relation to)

IT Radioelements, compounds
 Toxins
 RL: ANST (Analytical study)
 (conjugates, with **aptamers**)

IT Imaging
 (contrast agents, conjugates, with **aptamers**)

IT Oligosaccharides
 RL: ANST (Analytical study)
 (di-, **aptamer** oligonucleotide binding to)

IT Toxins
 RL: ANST (Analytical study)
 (diphtheria, **aptamer** oligonucleotide binding to)

IT Receptors
 RL: ANST (Analytical study)
 (epidermal growth factor/.alpha.-transforming growth factor, gene
 c-erbB, **aptamer** oligonucleotide binding to)

IT Receptors
 RL: ANST (Analytical study)
 (interleukin 1, **aptamer** oligonucleotide binding to)

IT Lymphokines and Cytokines
 RL: BIOL (Biological study)
 (interleukin 1, receptors, **aptamer** oligonucleotide binding
 to)

IT Lymphokines and Cytokines
 RL: BIOL (Biological study)
 (interleukins, **aptamer** oligonucleotide binding to)

IT Nucleotides, polymers
 RL: ANST (Analytical study)
 (oligo-, **aptamers**, for binding biomols.)

IT Proteins, specific or class
 RL: ANST (Analytical study)
 (transforming, **aptamer** oligonucleotide binding to)

IT Receptors
 Lymphokines and Cytokines
 RL: ANST (Analytical study)
 (tumor necrosis factor, **aptamer** oligonucleotide binding to)

IT Lymphokines and Cytokines
 RL: BIOL (Biological study)
 (tumor necrosis factor, receptors, **aptamer** oligonucleotide
 binding to)

IT Animal growth regulators
 RL: ANST (Analytical study)
 (.alpha.-transforming growth factors, gene c-erbB receptors,
aptamer oligonucleotide binding to)

IT Gene, animal
 RL: ANST (Analytical study)

(c-erbB2, protein product of, **aptamer** oligonucleotide binding to)

IT 9000-94-6, Antithrombin III 9001-12-1, Collagenase 9002-03-3, Dihydrofolate reductase 9004-06-2, Elastase 9027-44-5, Hydroxymethyl glutaryl CoA synthase 62031-54-3, Fibroblast growth factor 107231-12-9, Botulin 51-45-6, Histamine, biological studies
 RL: ANST (Analytical study)
 (**aptamer** oligonucleotide binding to)

IT 58-82-2, Bradykinin 551-11-1, Prostaglandin F2.alpha. 9001-29-0, Blood-coagulation factor X 9002-04-4, Thrombin
 RL: ANST (Analytical study)
 (**aptamer** oligonucleotide binding to, prepn. of)

IT 50-99-7, D-Glucose, biological studies 59-23-4, D-Galactose, biological studies 60-24-2, .beta.-Mercaptoethanol 617-04-9, .alpha.-Methyl-mannoside 1811-31-0, N-Acetylgalactosamine 3483-12-3, Dithiothreitol 7512-17-6, N-Acetylglucosamine
 RL: ANST (Analytical study)
 (in **aptamer** prepn.)

IT 62229-50-9, Epidermal growth factor
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (receptor, **aptamer** oligonucleotide binding to)

IT 145563-68-4 145751-88-8 146484-44-8 146484-45-9 146484-46-0
 146484-47-1 146484-48-2 146484-49-3 146484-50-6 146484-51-7
 146484-52-8 146484-53-9 146484-54-0 146484-55-1 146484-56-2
 146484-57-3 146484-58-4 146484-59-5 146484-61-9 146484-62-0
 146484-63-1 146484-64-2 146484-65-3 146484-66-4 146484-67-5
 146484-68-6 146484-69-7 146484-70-0 146484-71-1 146484-72-2
 146484-73-3 149460-11-7
 RL: ANST (Analytical study)
 (thrombin **aptamer**)

IT 9001-26-7, Prothrombin 9001-90-5, Plasmin
 RL: ANST (Analytical study)
 (thrombin **aptamer** binding activity for)

IT 77887-18-4
 RL: ANST (Analytical study)
 (thrombin-binding **aptamer** contg.)

IT 838-07-3, 5-Methyl-2'-deoxycytidine
 RL: ANST (Analytical study)
 (thrombin-binding **aptamers** contg.)

L6 ANSWER 107 OF 111 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 DUPLICATE 18
 AN 1994:295667 BIOSIS
 DN PREV199497308667
 TI Isolation and identification of **aptamers** from defibrotide that
 act as thrombin antagonists in vitro.
 AU Bracht, Franzpeter; Schroer, Karsten
 CS Institut fuer Pharmakologie, Heinrich-Heine-Universitaet Duesseldorf,
 D-40225 Duesseldorf, Germany
 SO Biochemical and Biophysical Research Communications, (1994) Vol. 200, No.
 2, pp. 933-937.
 CODEN: BBRCA9. ISSN: 0006-291X.
 DT Article
 LA English
 ED Entered STN: 13 Jul 1994
 Last Updated on STN: 24 Aug 1994
 AB This study was designed to isolate and identify **aptamer**
 sequences, acting as thrombin antagonists, from defibrotide, a
 single-stranded DNA fraction. Two different **aptamers** were
 identified: 5'GGTTGGATTGGTTGG-3' and 5'-GGTTGGATCGGTTGG-3'. A third
aptamer: 5'GGATGGATCGGTTGG-3' was found in the PCR
 product from the double-stranded defibrotide precursor. All
aptamers were potent inhibitors of thrombin-induced platelet
 aggregation, thromboxane biosynthesis, increase in cytosolic Ca++ and
 fibrin clot formation, effective concentrations being in the nanomolar
 range. There was no effect on U 46,619 (thromboxane mimetic) or
 collagen-induced responses. Similar effects were, obtained with
 unfractionated defibrotide while the "nonsense" oligonucleotide
 5'-GGTGGTGGTTGTGGT-3' was inactive. The data suggest that antithrombin
 effects of defibrotide are caused by **aptamers**.
 CC Cytology - Animal 02506
 Genetics - Animal 03506
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
 Biochemistry studies - Proteins, peptides and amino acids 10064
 Biophysics - Molecular properties and macromolecules 10506
 Cardiovascular system - Physiology and biochemistry 14504
 Cardiovascular system - Blood vessel pathology 14508
 Blood - Blood and lymph studies 15002
 In vitro cellular and subcellular studies 32600
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport
 and Circulation); Cardiovascular System (Transport and Circulation);
 Cell Biology; Genetics
 IT Chemicals & Biochemicals
 DEFIBROTIDE
 IT Miscellaneous Descriptors
 ANTIATHEROSCLEROTIC ACTIVITY; ANTITHROMBOTIC ACTIVITY
 ORGN Classifier
 Mammalia 85700
 Super Taxa
 Vertebrata; Chordata; Animalia
 Organism Name
 mammal
 Mammalia
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,
 Vertebrates
 RN 83712-60-1 (DEFIBROTIDE)

L6 ANSWER 106 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:291458 CAPLUS

DN 120:291458

ED Entered STN: 11 Jun 1994

TI The use of reversible chemical modification of the backbone of oligonucleotides for **PCR** amplification of **aptamers**

IN Bischofberger, Norbert; Fishback, James A.

PA Gilead Sciences, Inc., USA

SO PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07H021-00

ICS C07H019-10; C07H019-20; C12Q001-68; A61K031-70

CC 3-1 (Biochemical Genetics)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 9404548	A1	19940303	WO 1993-US7130	19930729
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9349948	A1	19940315	AU 1993-49948	19930729
PRAI	US 1992-932189	A	19920819		
	WO 1993-US7130	W	19930729		
AB	New aptamers with a region capable of specifically binding a target and at least one linking group where P(O)O or P(O)S is replaced by P(O)SR [R = substituted or unsubstituted C1-20 alkyl optionally contg. an ether (-O-) linkage, aryl, alkenyl, cycloalkyl, cycloalkenyl, arylakyl or R1YCOCR3R2 (R1, R2, R3 independently H, C1-9 alkyl; Y = a bond, O, S, NH)] are prepd. The prepn. of these aptamers includes treating recovered aptamers with base to convert the hydrocarbyl thioate linkages to phosphodiester linkages thereby forming a dehydrocarbylated aptamer prior to amplification. The modification is completely reversible allowing selection of the aptamers with protected backbones followed by deprotection and amplification of the selected sequences.				
ST	aptamer reversible chem modification backbone selection;				
	oligonucleotide backbone alkylation reversible				
IT	Deoxyribonucleic acids				
	RL: BIOL (Biological study)				
	(single-stranded, aptamers , reversible chem. modification of backbone in selection of)				
IT	Nucleotides, polymers				
	RL: BIOL (Biological study)				
	(oligo-, aptamers , reversible chem. modification of backbone in selection of)				
IT	Nucleotides, polymers				
	RL: BIOL (Biological study)				
	(oligo-, thiophosphate-linked, aptamers , reversible chem. modification of backbone in selection of)				
IT	135819-94-2	154977-93-2			
	RL: USES (Uses)				
	(reversible alkylation of thioate linkage of, reversible modification of backbone in selection of aptamers in relation to)				
IT	106-95-6, Allyl bromide, reactions	556-56-9, Allyl iodide	620-05-3, Benzyl iodide		
	RL: RCT (Reactant); RACT (Reactant or reagent)				
	(reversible alkylation of thioate linkages of oligonucleotides with, reversible modification of backbone in selection of aptamers in relation to)				

L6 ANSWER 105 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:114948 CAPLUS
 DN 124:167400
 ED Entered STN: 23 Feb 1996
 TI In vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6
 AU Kim, Meehyein; Jeoung, Yeon-Hee; Lee, Seog Jae; Choi, Inpyo; Pyun, Kwang-Ho; Lee, Younghoon
 CS Dep. of Chemistry, Korea Advanced Inst. Science and Technology, Taejon, 305-701, S. Korea
 SO Molecules and Cells (1995), 5(6), 555-62
 CODEN: MOCEEK; ISSN: 1016-8478
 PB Korean Society of Molecular Biology
 DT Journal
 LA English
 CC 3-4 (Biochemical Genetics)
 AB IL-6 is known to inhibit growth and induce differentiation of several myeloid leukemia cell lines. With the recombinant human interleukin-6 (IL-6) as a target protein, DNA **aptamers** specifically binding to IL-6 were isolated from a random oligodeoxyribonucleotide pool. A large pool of 96-mer oligodeoxyribonucleotides, made up of 60 bases of random sequences flanked by the defined regions of primer binding sites at the 5' and 3' ends, was synthesized. This randomly generated oligodeoxyribonucleotide pool was denatured to generate single-stranded DNA and subjected to in vitro selection with affinity chromatog. and in vitro amplification with polymerase chain reaction (PCR) for enrichment in single-stranded DNA **aptamers** specifically binding to IL-6. Multiple rounds of successive affinity chromatog. and PCR resulted in the continued purifn. of binding species. The gel retardation expt. showed that **aptamers** had affinity to IL-6 with dissochn. consts. of the order of magnitude of 10^{-6} M. The sequences of the **aptamers** were identified. A homol. search revealed that they were categorized into at least four groups according to the consensus sequences among them.
 ST interleukin 6 DNA binding **aptamer**
 IT Deoxyribonucleic acids
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (aptamer; in vitro selection of DNA **aptamers** binding to human interleukin-6)
 IT Deoxyribonucleic acid sequences
 (in vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6)
 IT Lymphokines and Cytokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (interleukin 6, in vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6)

L6 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:392082 CAPLUS
 DN 129:38128
 ED Entered STN: 26 Jun 1998
 TI Thrombin-specific **aptamers** and methods for detection or
 purification of thrombin
 IN Griffin, Linda; Albrecht, Glenn; Latham, John; Leung, Lawrence; Vermaas,
 Eric; Toole, John J.
 PA Gilead Sciences, Inc., USA
 SO U.S., 115 pp., Cont. of U. S. Ser. No. 934,387, abandoned.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM C12Q001-68
 ICS C07K001-14; C07H021-04; C07H021-02
 NCL 435006000
 CC 7-8 (Enzymes)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5756291	A	19980526	US 1995-484192	19950607
PRAI	US 1992-934387		19920821		

AB Methods for detection of thrombin using labeled DNA which specifically
 binds to thrombin (**aptamers**) and methods for purifn. of thrombin
 using the unlabeled **aptamers** are disclosed. A method for
 identifying oligomer sequences, optionally comprising modified bases,
 which specifically bind target mols. such as serum proteins, kinins,
 eicosanoids and extracellular proteins is described. The method is used
 to generate **aptamers** that bind to serum Factor X, PDGF, FGF,
 ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface mols.
 The technique involves complexation of the target mol. with a mixt. of
 oligonucleotides contg. random sequences and sequences which serve as
 primer for **PCR** under conditions wherein a complex is formed with
 the specifically binding sequences, but not with the other members of the
 oligonucleotide mixt. The complex is then sepd. from uncomplexed
 oligonucleotides and the complexed members of the oligonucleotide mixt.
 are recovered from the sepd. complex using the polymerase chain reaction.
 The recovered oligonucleotides may be sequenced, and successive rounds of
 selection using complexation, sepn., amplification and recovery can be
 employed. The oligonucleotides can be used for therapeutic and diagnostic
 purposes and for generating secondary **aptamers**.
 ST **aptamer** thrombin detection purifn
 IT Selectins
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (E-; thrombin-specific **aptamers** and methods for detection or
 purifn. of thrombin)
 IT Cell adhesion molecules
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (ICAM-1 (intercellular adhesion mol. 1); thrombin-specific
aptamers and methods for detection or purifn. of thrombin)
 IT Cell adhesion molecules
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (VCAM-1; thrombin-specific **aptamers** and methods for detection
 or purifn. of thrombin)
 IT Nucleic acids
 Oligonucleotides
 RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
 PREP (Preparation); PROC (Process); USES (Uses)

(**aptamers**; thrombin-specific **aptamers** and methods
for detection or purifn. of thrombin)

IT CD4 (antigen)
Interleukin 1
neu (receptor)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)

(thrombin-specific **aptamers** and methods for detection or
purifn. of thrombin)

IT 126320-34-1P 145563-68-4P 146484-44-8P 146484-45-9P 146484-46-0P
146484-47-1P 146484-73-3P 207997-14-6P 207997-15-7P 208057-35-6P
208057-36-7P 208057-37-8P 208057-38-9P 208057-39-0P 208057-40-3P
208057-41-4P 208057-42-5P 208057-43-6P 208057-44-7P 208057-45-8P
208057-46-9P 208057-47-0P 208057-48-1P 208057-49-2P 208057-50-5P
208197-60-8P 208197-61-9P 208197-62-0P 208197-63-1P 208197-64-2P
208197-65-3P 208197-66-4P 208197-67-5P

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); PROC (Process); USES (Uses)

(thrombin-binding **aptamer**; thrombin-specific **aptamers**
and methods for detection or purifn. of thrombin)

IT 9002-04-4P, Thrombin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study,
unclassified); PUR (Purification or recovery); ANST (Analytical study);
BIOL (Biological study); PREP (Preparation); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or
purifn. of thrombin)

IT 58-82-2, Bradykinin 9001-29-0, Blood-coagulation factor X 106096-93-9,
Basic fibroblast growth factor 123123-44-4

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)

(thrombin-specific **aptamers** and methods for detection or
purifn. of thrombin)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Anon; WO 9102750 2000 CAPLUS
- (2) Anon; WO 9119813 2000 CAPLUS
- (3) Aoki; US 4748156 1988 CAPLUS
- (4) Blackwell; Science 1990, V250, P1104 CAPLUS
- (5) Blackwell; Science 1990, V250, P1149 CAPLUS
- (6) Bock; Nature 1992, V356, P564
- (7) Chittenden; Cell 1991, V65, P1073 CAPLUS
- (8) Ellington; Nature 1990, V346, P818 CAPLUS
- (9) Ellington; Nature 1992, V355, P850 CAPLUS
- (10) Ferns; Science 1992, V253, P1129
- (11) Gold; US 5270163 1993 CAPLUS
- (12) Huynh-Dinh; PNAS 1985, V32, P7510
- (13) Isobe, M; Science 1992, V255, P425
- (14) Kadonaga; PNAS, USA 1986, V83, P5889 CAPLUS
- (15) Kavanaugh; J Biol Chem 1988, V263, P8470 CAPLUS
- (16) Kinzler; Mol Cell Biol 1990, V10, P634 CAPLUS
- (17) Kinzler; Nucleic Acids Res 1989, V17, P3645 CAPLUS
- (18) Kirk-Othmer; "Encyclopedia of Chemical Technology," 3rd Ed 1979, V6, P35
- (19) Libby; NEJM 1988, V318, P1493 MEDLINE
- (20) Lindner; Circulation Research 1991, V68, P106 CAPLUS
- (21) Mann; Meth Enzymol 1981, V80, P286 CAPLUS
- (22) Oliphant; Mol Cell Biol 1989, V9(7), P2944 CAPLUS
- (23) Oliphant; Nucl Acids Res 1988, V16(15), P7673 CAPLUS
- (24) Oppenheimer-Marks; Immunol 1991, V147, P2913 CAPLUS
- (25) Riordan; Nature 1992, V350, P442
- (26) Saiki; Science 1988, V239, P487 CAPLUS
- (27) Springer, T; Nature 1990, V346, P425 CAPLUS

- (28) Straunton; Cell 1990, V61, P243
- (29) Thiesen; Nucleic Acids Res 1990, V18(11), P3203 CAPLUS
- (30) Tuerk; Science 1990, V249, P505 CAPLUS
- (31) Ullman; Enzyme-Immunoassay 1988, V5, P105
- (32) van Lente; Enzyme-Immunoassay 1988, V6, P135

L6 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:392082 CAPLUS
 DN 129:38128
 ED Entered STN: 26 Jun 1998
 TI Thrombin-specific **aptamers** and methods for detection or
 purification of thrombin
 IN Griffin, Linda; Albrecht, Glenn; Latham, John; Leung, Lawrence; Vermaas,
 Eric; Toole, John J.
 PA Gilead Sciences, Inc., USA
 SO U.S., 115 pp., Cont. of U. S. Ser. No. 934,387, abandoned.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM C12Q001-68
 ICS C07K001-14; C07H021-04; C07H021-02
 NCL 435006000
 CC 7-8 (Enzymes)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	US 5756291	A	19980526	US 1995-484192	19950607
PRAI	US 1992-934387		19920821		

AB Methods for detection of thrombin using labeled DNA which specifically
 binds to thrombin (**aptamers**) and methods for purifn. of thrombin
 using the unlabeled **aptamers** are disclosed. A method for
 identifying oligomer sequences, optionally comprising modified bases,
 which specifically bind target mols. such as serum proteins, kinins,
 eicosanoids and extracellular proteins is described. The method is used
 to generate **aptamers** that bind to serum Factor X, PDGF, FGF,
 ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface mols.
 The technique involves complexation of the target mol. with a mixt. of
 oligonucleotides contg. random sequences and sequences which serve as
 primer for **PCR** under conditions wherein a complex is formed with
 the specifically binding sequences, but not with the other members of the
 oligonucleotide mixt. The complex is then sepd. from uncomplexed
 oligonucleotides and the complexed members of the oligonucleotide mixt.
 are recovered from the sepd. complex using the polymerase chain reaction.
 The recovered oligonucleotides may be sequenced, and successive rounds of
 selection using complexation, sepn., amplification and recovery can be
 employed. The oligonucleotides can be used for therapeutic and diagnostic
 purposes and for generating secondary **aptamers**.

ST **aptamer** thrombin detection purifn

IT Selectins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(E-; thrombin-specific **aptamers** and methods for detection or
 purifn. of thrombin)

IT Cell adhesion molecules

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(ICAM-1 (intercellular adhesion mol. 1); thrombin-specific
aptamers and methods for detection or purifn. of thrombin)

IT Cell adhesion molecules

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(VCAM-1; thrombin-specific **aptamers** and methods for detection
 or purifn. of thrombin)

IT Nucleic acids

Oligonucleotides

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
 PREP (Preparation); PROC (Process); USES (Uses)

(**aptamers**; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT CD4 (antigen)
Interleukin 1
neu (receptor)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT 126320-34-1P 145563-68-4P 146484-44-8P 146484-45-9P 146484-46-0P
146484-47-1P 146484-73-3P 207997-14-6P 207997-15-7P 208057-35-6P
208057-36-7P 208057-37-8P 208057-38-9P 208057-39-0P 208057-40-3P
208057-41-4P 208057-42-5P 208057-43-6P 208057-44-7P 208057-45-8P
208057-46-9P 208057-47-0P 208057-48-1P 208057-49-2P 208057-50-5P
208197-60-8P 208197-61-9P 208197-62-0P 208197-63-1P 208197-64-2P
208197-65-3P 208197-66-4P 208197-67-5P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(thrombin-binding **aptamer**; thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT 9002-04-4P, Thrombin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

IT 58-82-2, Bradykinin 9001-29-0, Blood-coagulation factor X 106096-93-9, Basic fibroblast growth factor 123123-44-4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(thrombin-specific **aptamers** and methods for detection or purifn. of thrombin)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Anon; WO 9102750 2000 CAPLUS
- (2) Anon; WO 9119813 2000 CAPLUS
- (3) Aoki; US 4748156 1988 CAPLUS
- (4) Blackwell; Science 1990, V250, P1104 CAPLUS
- (5) Blackwell; Science 1990, V250, P1149 CAPLUS
- (6) Bock; Nature 1992, V356, P564
- (7) Chittenden; Cell 1991, V65, P1073 CAPLUS
- (8) Ellington; Nature 1990, V346, P818 CAPLUS
- (9) Ellington; Nature 1992, V355, P850 CAPLUS
- (10) Ferns; Science 1992, V253, P1129
- (11) Gold; US 5270163 1993 CAPLUS
- (12) Huynh-Dinh; PNAS 1985, V32, P7510
- (13) Isobe, M; Science 1992, V255, P425
- (14) Kadonaga; PNAS, USA 1986, V83, P5889 CAPLUS
- (15) Kavanaugh; J Biol Chem 1988, V263, P8470 CAPLUS
- (16) Kinzler; Mol Cell Biol 1990, V10, P634 CAPLUS
- (17) Kinzler; Nucleic Acids Res 1989, V17, P3645 CAPLUS
- (18) Kirk-Othmer; "Encyclopedia of Chemical Technology," 3rd Ed 1979, V6, P35
- (19) Libby; NEJM 1988, V318, P1493 MEDLINE
- (20) Lindner; Circulation Research 1991, V68, P106 CAPLUS
- (21) Mann; Meth Enzymol 1981, V80, P286 CAPLUS
- (22) Oliphant; Mol Cell Biol 1989, V9(7), P2944 CAPLUS
- (23) Oliphant; Nucl Acids Res 1988, V16(15), P7673 CAPLUS
- (24) Oppenheimer-Marks; Immunol 1991, V147, P2913 CAPLUS
- (25) Riordan; Nature 1992, V350, P442
- (26) Saiki; Science 1988, V239, P487 CAPLUS
- (27) Springer, T; Nature 1990, V346, P425 CAPLUS

- (28) Straunton; Cell 1990, V61, P243
- (29) Thiesen; Nucleic Acids Res 1990, V18(11), P3203 CAPLUS
- (30) Tuerk; Science 1990, V249, P505 CAPLUS
- (31) Ullman; Enzyme-Immunoassay 1988, V5, P105
- (32) van Lente; Enzyme-Immunoassay 1988, V6, P135

L6 ANSWER 105 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:114948 CAPLUS
 DN 124:167400
 ED Entered STN: 23 Feb 1996
 TI In vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6
 AU Kim, Meehyein; Jeoung, Yeon-Hee; Lee, Seog Jae; Choi, Inpyo; Pyun, Kwang-Ho; Lee, Younghoon
 CS Dep. of Chemistry, Korea Advanced Inst. Science and Technology, Taejon, 305-701, S. Korea
 SO Molecules and Cells (1995), 5(6), 555-62
 CODEN: MOCEEK; ISSN: 1016-8478
 PB Korean Society of Molecular Biology
 DT Journal
 LA English
 CC 3-4 (Biochemical Genetics)
 AB IL-6 is known to inhibit growth and induce differentiation of several myeloid leukemia cell lines. With the recombinant human interleukin-6 (IL-6) as a target protein, DNA **aptamers** specifically binding to IL-6 were isolated from a random oligodeoxyribonucleotide pool. A large pool of 96-mer oligodeoxyribonucleotides, made up of 60 bases of random sequences flanked by the defined regions of primer binding sites at the 5' and 3' ends, was synthesized. This randomly generated oligodeoxyribonucleotide pool was denatured to generate single-stranded DNA and subjected to in vitro selection with affinity chromatog. and in vitro amplification with polymerase chain reaction (PCR) for enrichment in single-stranded DNA **aptamers** specifically binding to IL-6. Multiple rounds of successive affinity chromatog. and PCR resulted in the continued purifn. of binding species. The gel retardation expt. showed that **aptamers** had affinity to IL-6 with dissochn. consts. of the order of magnitude of 10^{-6} M. The sequences of the **aptamers** were identified. A homol. search revealed that they were categorized into at least four groups according to the consensus sequences among them.
 ST interleukin 6 DNA binding **aptamer**
 IT Deoxyribonucleic acids
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (aptamer; in vitro selection of DNA **aptamers** binding to human interleukin-6)
 IT Deoxyribonucleic acid sequences
 (in vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6)
 IT Lymphokines and Cytokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (interleukin 6, in vitro selection of DNA **aptamers** binding to the recombinant human interleukin-6)

L6 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1998:392082 CAPLUS
 DN 129:38128
 ED Entered STN: 26 Jun 1998
 TI Thrombin-specific **aptamers** and methods for detection or
 purification of thrombin
 IN Griffin, Linda; Albrecht, Glenn; Latham, John; Leung, Lawrence; Vermaas,
 Eric; Toole, John J.
 PA Gilead Sciences, Inc., USA
 SO U.S., 115 pp., Cont. of U. S. Ser. No. 934,387, abandoned.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM C12Q001-68
 ICS C07K001-14; C07H021-04; C07H021-02
 NCL 435006000
 CC 7-8 (Enzymes)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5756291	A	19980526	US 1995-484192	19950607
PRAI	US 1992-934387		19920821		

AB Methods for detection of thrombin using labeled DNA which specifically
 binds to thrombin (**aptamers**) and methods for purifn. of thrombin
 using the unlabeled **aptamers** are disclosed. A method for
 identifying oligomer sequences, optionally comprising modified bases,
 which specifically bind target mols. such as serum proteins, kinins,
 eicosanoids and extracellular proteins is described. The method is used
 to generate **aptamers** that bind to serum Factor X, PDGF, FGF,
 ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface mols.
 The technique involves complexation of the target mol. with a mixt. of
 oligonucleotides contg. random sequences and sequences which serve as
 primer for **PCR** under conditions wherein a complex is formed with
 the specifically binding sequences, but not with the other members of the
 oligonucleotide mixt. The complex is then sepd. from uncomplexed
 oligonucleotides and the complexed members of the oligonucleotide mixt.
 are recovered from the sepd. complex using the polymerase chain reaction.
 The recovered oligonucleotides may be sequenced, and successive rounds of
 selection using complexation, sepn., amplification and recovery can be
 employed. The oligonucleotides can be used for therapeutic and diagnostic
 purposes and for generating secondary **aptamers**.
 ST **aptamer** thrombin detection purifn
 IT Selectins
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (E; thrombin-specific **aptamers** and methods for detection or
 purifn. of thrombin)
 IT Cell adhesion molecules
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (ICAM-1 (intercellular adhesion mol. 1); thrombin-specific
aptamers and methods for detection or purifn. of thrombin)
 IT Cell adhesion molecules
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (VCAM-1; thrombin-specific **aptamers** and methods for detection
 or purifn. of thrombin)
 IT Nucleic acids
 Oligonucleotides
 RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
 PREP (Preparation); PROC (Process); USES (Uses)

- (28) Straunton; Cell 1990, V61, P243
- (29) Thiesen; Nucleic Acids Res 1990, V18(11), P3203 CAPLUS
- (30) Tuerk; Science 1990, V249, P505 CAPLUS
- (31) Ullman; Enzyme-Immunoassay 1988, V5, P105
- (32) van Lente; Enzyme-Immunoassay 1988, V6, P135

L6 ANSWER 110 OF 111 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1993:164224 CAPLUS
 DN 118:164224
 ED Entered STN: 01 May 1993
 TI **Aptamers** specific for thrombin and methods of use
 IN Toole, John J.; Griffin, Linda C.; Bock, Louis C.; Latham, John A.;
 Krawczyk, Steven
 PA Gilead Sciences, Inc., USA
 SO PCT Int. Appl., 83 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C12Q001-68
 ICS C07H015-12; C07H017-00
 CC 7-3 (Enzymes)
 Section cross-reference(s): 1, 3, 9, 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9214842	A1	19920903	WO 1992-US1367	19920221
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
	CA 2104698	AA	19920822	CA 1992-2104698	19920221
	AU 9214560	A1	19920915	AU 1992-14560	19920221
	US 5582981	A	19961210	US 1994-234613	19940428
	US 5840867	A	19981124	US 1994-237973	19940503

PRAI US 1991-658849 19910221
 US 1991-659981 19910221
 US 1991-744870 19910814
 US 1991-745215 19910814
 US 1991-787921 19911106
 WO 1992-US1367 19920221

AB Single-stranded thrombin **aptamers** (oligonucleotides that bind specifically to thrombin) are obtained that inhibit both its catalytic activity and its platelet-aggregating activity. The **aptamers**, which show little or no immunogenicity, may be used in treatment or prophylaxis of vascular diseases, inflammatory responses, cancer-related hypercoagulable states, etc., as well as for in vitro or in vivo imaging, diagnosis, thrombin detection and purifn., blood storage, and coating of implant devices. The oligomers are identified by complexation of support-bound thrombin with a mixt. of oligonucleotides contg. random sequences under conditions wherein a complex is formed with the specifically binding sequences but not with other members of the mixt. The thrombin-oligonucleotide complexes are then sepd. from the support and the uncomplexed oligonucleotides, the complexes are dissocd., and the **aptamers** are amplified by std. techniques. The **aptamers** may contain modified bases, sugars, or sugar linkages. Thus, deoxyoligonucleotides were synthesized which contained a random 60-mer sequence between 2 specific 18-mer sequences. The oligomers were heat denatured and applied to a column of thrombin bound to Con A-agarose, and bound oligomers were eluted with buffer contg. thrombin and amplified by **PCR** using the 5' 18-mer and the complement to the 3' 18-mer as primers and the random 96-mer as template. Active clones bound thrombin in the presence of the fibrinogen substrate and contained a consensus sequence, GGNTGGNzGGNTGG (z = 2-5) or a close variant thereof, responsible for thrombin affinity.

ST thrombin oligonucleotide binding

IT Drug delivery systems

(**aptamer** conjugates, thrombin-binding and -inhibiting)

IT Albumins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(binding of, by oligonucleotides)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(immobilized, complexes with thrombin, in prepn. of thrombin-binding and -inhibiting oligonucleotides)

IT DNA
Oligodeoxyribonucleotides, polymers
RNA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin binding and inhibition by)

IT Anticoagulants
(thrombin-binding and -inhibiting oligonucleotides)

IT Radionuclides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-binding and -inhibiting oligonucleotides labeled with)

IT Monosaccharides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thrombin-oligonucleotide complexes dissocn. from immobilized lectin with)

IT Ligands
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(conjugated, with thrombin-binding and -inhibiting oligonucleotides)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(conjugates, with thrombin-binding and -inhibiting oligonucleotides)

IT Imaging agents
(contrast, thrombin-binding and -inhibiting oligonucleotides labeled with)

IT Artery, disease
(coronary, restenosis, treatment of, with thrombin-binding and -inhibiting oligonucleotides)

IT Structure-activity relationship
(thrombin-inhibiting, of oligonucleotides)

IT 9002-04-4, Thrombin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(binding and inhibition of, by oligonucleotides)

IT 9001-26-7, Blood-coagulation factor II 9001-90-5, Plasmin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(binding of, by oligonucleotides)

IT 9002-04-4D, Thrombin, lectin complexes 9012-36-6D, Agarose, Con A conjugates, complexes with thrombin 11028-71-0D, Concanavalin A, thrombin complexes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(in thrombin-binding and -inhibiting oligonucleotides prepn.)

IT 554-01-8 77887-18-4 84558-94-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(oligonucleotides contg., thrombin binding and inhibition by)

IT 145563-68-4 146484-44-8 146484-45-9 146484-46-0 146484-47-1
146484-48-2 146484-49-3 146484-50-6 146484-51-7 146484-52-8
146484-53-9 146484-54-0 146484-55-1 146484-56-2 146484-57-3